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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/047,855

01/15/2002

Lillian Wei-Ming Chiang

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MILLENNIUM PHARMACEUTICALS, INC.

40 Landsdowne Street
CAMBRIDGE, MA 02139

EXAMINER

HOLLERAN, ANNE L

ART UNIT

PAPER NUMBER

1642

DATE MAILED: 04/06/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/047,855

Applicant(s)

CHIANG, LILLIAN WEI-MING

Examiner

Anne Holleran

Art Unit

1642

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 1 MONTH(S) FROM
THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-23 is/are pending in the application.
- 4a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☐ Claim(s) ____ is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☒ Claim(s) 1-23 are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- 1) ☐ Certified copies of the priority documents have been received.
 - 2) ☐ Certified copies of the priority documents have been received in Application No. ____.
 - 3) ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date ____.
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date ____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: ____.

DETAILED ACTION

1. Prior to setting forth the restriction requirement, it is noted that the claims recite improper Markush Groups. M.P.E.P. 803.02 states that: Since the decisions in *In re Weber*, 580 F.2d 455, 198 USPQ 328 (CCPA 1978); and *In re Haas*, 580 F.2d 461, 198 USPQ 334 (CCPA 1978), it is improper for the Office to refuse to examine that which applicants regard as their invention, *unless the subject matter in a claim lacks unity of invention* [emphasis added], *In re Harnish*, 631 F.2d 716, 206 USPQ 300 (CCPA 1980); and *Ex parte Hozumi*, 3 USPQ2d 1059 (Bd. Pat. App. & Int. 1984). Broadly, unity of invention exists where compounds included within a Markush group (1) share a common utility and (2) share a substantial structural feature disclosed as being essential to that utility. In the instant case, the products are polynucleotides that encode separate and distinct polypeptide products (i.e. SEQ ID NO: 1 and SEQ ID NO: 3), which differ in structure and origin to such an extent that non-coextensive searches are required, and that the polynucleotides, polypeptides encoded by the polynucleotides and antibodies that bind to the polypeptides are considered to lack a substantial structural feature disclosed as being essential to the disclosed utility. As such, the structurally different polynucleotides, polypeptides and antibodies have been restricted each from the other.

Election/Restrictions

2. Restriction to one of the following inventions is required under 35 U.S.C. 121:
- I. Claims 1-7, 12, 13 and 19, to the extent the claims are drawn to polynucleotides encoding SEQ ID NO: 1, encode fragments of SEQ ID NO: 1, encodes a variant of SEQ ID NO: 1, polynucleotides that are complementary to polynucleotides

encoding SEQ ID NO: 1, vectors comprising said polynucleotide sequences, host cells comprising said polynucleotide sequences and methods of making SEQ ID NO: 1, and kits comprising said polynucleotides, classified in class 536, subclass 23.5, and in class 435, subclasses 69.1, 320.1, 325.

- II. Claims 1-7, 12, 13, 19, to the extent the claims are drawn to polynucleotides encoding SEQ ID NO: 3, encode fragments of SEQ ID NO: 3, encodes a variant of SEQ ID NO: 3, polynucleotides that are complementary to polynucleotides encoding SEQ ID NO: 3, vectors comprising said polynucleotide sequences, host cells comprising said polynucleotide sequences and methods of making SEQ ID NO: 3, and kits comprising said polynucleotides classified in class 536, subclass 23.5, and in class 435, subclasses 69.1, 320.1, 325.
- III. Claims 8-10, to the extent the claims are drawn to polypeptides of SEQ ID NO: 1, fragments of SEQ ID NO: 1, variants of SEQ ID NO: 1, classified in class 530, subclass 350.
- IV. Claims 8-10, to the extent the claims are drawn to polypeptides of SEQ ID NO: 3, fragments of SEQ ID NO: 3, variants of SEQ ID NO: 3, classified in class 530, subclass 350.
- V. Claims 11 and 16, to the extent the claims are drawn to antibodies and kits, where the antibodies bind to polypeptides of SEQ ID NO: 1, classified in class 530, subclass 387.1.

- VI. Claims 11 and 16, to the extent the claims are drawn to antibodies and kits, where the antibodies bind to polypeptides of SEQ ID NO: 3, classified in class 530, subclass 387.1.
- VII. Claims 14 and 15, to the extent the claims are drawn to methods for the detection of the presence of a polypeptide of SEQ ID NO: 1, classified in class 435 subclass 7.1.
- VIII. Claims 14 and 15, to the extent the claims are drawn to methods for the detection of the presence of a polypeptide of SEQ ID NO: 3, classified in class 435 subclass 7.1.
- IX. Claims 17 and 18, to the extent the claims are drawn to methods for the detection of the presence of nucleic acids encoding a polypeptide of SEQ ID NO: 1, classified in class 435, subclass 6.
- X. Claims 17 and 18, to the extent the claims are drawn to methods for the detection of the presence of nucleic acids encoding a polypeptide of SEQ ID NO: 3, classified in class 435, subclass 6.
- XI. Claims 20 and 21, to the extent the claims are drawn to methods for the identification of compounds that bind to a polypeptide of SEQ ID NO: 1, classified in class 435, subclass 4, class 436, subclass 501.
- XII. Claims 20 and 21, to the extent the claims are drawn to methods for the identification of compounds that bind to a polypeptide of SEQ ID NO: 3, classified in class 436, subclass 501.

- XIII. Claim 22, to the extent the claim is drawn to a method for modulating the activity of a polypeptide of SEQ ID NO: 1, classified in class 514, subclass 2.
- XIV. Claim 22, to the extent the claim is drawn to a method for modulating the activity of a polypeptide of SEQ ID NO: 3, classified in class 514, subclass 2.
- XV. Claim 23, to the extent the claim is drawn to a method for identifying a compound that modulates the activity of a polypeptide of SEQ ID NO: 1, class 435, subclass 4.
- XVI. Claim 23, to the extent the claim is drawn to a method for identifying a compound that modulates the activity of a polypeptide of SEQ ID NO: 3, class 435, subclass 4.

3. The inventions are distinct, each from the other because of the following reasons:
Inventions I-VI are patentably distinct products.

The polypeptides of groups III and IV and polynucleotides of groups I and II are patentably distinct inventions for the following reasons. Polypeptides, which are composed of amino acids, and polynucleotides, which are composed of purine and pyrimidine units, are structurally distinct molecules; any relationship between a polynucleotide and polypeptide is dependent upon the information provided by the nucleic acid sequence open reading frame as it corresponds to the primary amino acid sequence of the encoded polypeptide. In the present claims, a polynucleotides of groups I and II do not necessarily encode a polypeptide of group III or group IV. For example, a nucleotide sequence of claim 1(a) having 70% sequence identity with the nucleotide sequence of SEQ ID NO: 2 does not encode the polypeptide of SEQ ID NO:

1 or SEQ ID NO: 3. Similarly, the nucleic acid molecule of claim 1(k) is complementary to the coding sequence, and therefore would not encode the polypeptide of group III or of group IV. In addition, while a polypeptide of group III or IV can be made by methods using some, but not all, of the polynucleotides that fall within the scope of group I or group II, it can also be recovered from a natural source using biochemical means. For instance, the polypeptide can be isolated using affinity chromatography. For these reasons, the inventions of groups I and II are patentably distinct from the inventions of groups III and IV.

Furthermore, searching the inventions of either of groups I and II together with either of groups III and IV would impose a serious search burden. In the instant case, the search of the polypeptides and the polynucleotides are not coextensive. The inventions of groups I and II versus the inventions of groups III and IV have a separate status in the art as shown by their different classifications. In cases such as this one where descriptive sequence information is provided, the sequences are searched in appropriate databases. There is search burden also in the non-patent literature. Prior to the concomitant isolation and expression of the sequence of interest there may be journal articles devoted solely to polypeptides that would not have described the polynucleotide. Similarly, there may have been "classical" genetics papers that had no knowledge of the polypeptide but spoke to the gene. Searching, therefore is not coextensive. In addition, the polypeptide claims include polypeptides having 70% identity to the sequence identified. This search requires an extensive analysis of the art retrieved in a sequence search and will require an in-depth analysis of technical literature. The scope of polynucleotides as claimed extend beyond the polynucleotide that encodes the claimed polypeptides as explained above; furthermore, a search of the nucleic acid molecules of claim 1(a) or 1(b) would require an

oligonucleotide search, which is not likely to result in relevant art with respect to the polypeptides of groups III and IV. As such, it would be burdensome to search the inventions of groups I or II together with either of groups III or IV.

The polypeptides of group III and IV and the antibodies of group V and VI are patentably distinct for the following reasons:

While the inventions of both groups III and IV and both groups V and VI are polypeptides, in this instance the polypeptide of groups III and IV is a single chain molecule that has some biological, whereas the polypeptides of group V and VI encompasses antibodies including IgG which comprises 2 heavy and 2 light chains containing constant and variable regions, and including framework regions which act as a scaffold for the 6 complementarity determining regions (CDRs) that function to bind an epitope. Thus, the polypeptides of groups III and IV and the antibodies of groups V and VI are structurally distinct molecules. Therefore the polypeptide and antibody are patentably distinct.

Furthermore, searching the inventions of group III and IV with either of groups V and VI would impose a serious search burden. The inventions have a separate status in the art as shown by their different classifications. A polypeptide and an antibody that binds to the polypeptide require different searches. An amino acid sequence search of the full-length protein is necessary for a determination of novelty and unobviousness of the protein. However, such a search is not required to identify the antibodies of groups V or VI. Furthermore, antibodies that bind to an epitope of a polypeptides of group III and IV may be known even if a polypeptide of groups III and IV are novel. In addition, the technical literature search for the polypeptides of group III and

IV and the antibodies of groups V and VI are not coextensive, e.g., antibodies may be characterized in the technical literature prior to discovery of or sequence of their binding target.

The polynucleotides of groups I and II and the antibodies of groups V and VI are patentably distinct for the following reasons. The antibodies of groups V and VI include, for example, IgG molecules which comprise 2 heavy and 2 light chains containing constant and variable regions, and including framework regions which act as a scaffold for the 6 complementarity determining regions (CDRs). Polypeptides, such as the antibodies of groups V and VI, which are composed of amino acids, and polynucleotides, which are composed of nucleic acids, are structurally distinct molecules; any relationship between a polynucleotide and polypeptide is dependent upon the information provided by the nucleic acid sequence open reading frame as it corresponds to the primary amino acid sequence of the encoded polypeptide. In the present claims, a polynucleotides of groups I and II will not encode an antibody from either of groups V and VI, and the antibodies of groups V and VI cannot be encoded by a polynucleotides of groups I and II. Therefore the antibodies and polynucleotides are patentably distinct.

The antibody and polynucleotide inventions have a separate status in the art as shown by their different classifications. Furthermore, searching the inventions of groups I and II with either of groups V and VI would impose a serious search burden since a search of the polynucleotides of groups I and II would not be used to determine the patentability of an antibody of either of groups V and VI, and vice-versa.

Inventions VII-XVI are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). The instant specification does not disclose that these methods would be used together. The methods of detecting the presence of a polypeptide using an antibody (groups VII and VIII), the methods of detecting a nucleic acid using a polynucleotide (groups IX and X), the methods of identifying a compound using a polypeptide (groups XI and XII), the methods of modulating the activity of polypeptide using a compound that binds to a polypeptide (groups XIII and XIV), and the methods of identifying a compound that modulates the activity of a polypeptide using a polypeptide (groups XV and XVI) are all unrelated because they comprise distinct steps and utilize different products which demonstrates that each method has a different mode of operation. Each invention performs this function using a structurally and functionally divergent material. Moreover, the methodologies and materials necessary for each of the methods differs. For detection of a polypeptide using an antibody or a binding agent, quantitation of a labeled binding agent or labeled antibody may be used. For detection of a nucleic acid using the polypeptide, hybridization methods are used. For identification of a compound that binds to the polypeptide, the polypeptide is used to test various compounds. For modulation of the activity of a polypeptide, a binding agent or small molecule that inhibits polypeptide activity is used. For identification of a compound that modulates the activity of a polypeptide, the polypeptide's activity is measured. Therefore, each method is divergent in materials and steps. For these reasons the Inventions VII-XVI are patentably distinct.

Furthermore, the distinct steps and products require separate and distinct searches. The inventions of Groups VII-XVI have a separate status in the art as shown by their different classifications. As such, it would be burdensome to search the inventions of Groups VII-XVI together.

Inventions I and II and inventions IX and X, respectively, are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the polynucleotides of groups I and II can be used to make recombinant proteins as opposed to its use in detecting a polynucleotide.

Searching the inventions of Groups I or II together with IX or X would impose serious search burden. The inventions of Groups I and II and IX and X have a separate status in the art as shown by their different classifications. Moreover, in the instant case, the search for the polynucleotides and the methods of detecting a nucleic acid using a polynucleotide are not coextensive. Groups I and II encompasses molecules which are claimed in terms of percent identity with regard to a reference sequence, which are not required for the search of Groups IX or X. In contrast, the search for group IX or X would require a text search for methods of detecting nucleic acids. Prior art that teaches a polynucleotide that is 70% identical to a sequence would not necessarily be applicable to the methods of detecting a nucleic acid. Moreover, even if the polynucleotide product were known, the method of diagnosis using the product may be novel and unobvious in view of the preamble or active steps.

Inventions III and IV and inventions XI, XII, XV or XVI are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the polypeptides can be used either in a methods to identify compounds that bind to a polypeptide or to methods for identifying a compound that modulates the activity of a compound. These are materially different processes because one method requires detection of bound complexes and the other requires the quantification of polypeptide activity.

Searching the inventions of Groups III and IV and inventions XI, XII, XV or XVI together would impose serious search burden. The inventions of Groups III and IV and inventions XI, XII, XV or XVI have a separate status in the art as shown by their different classifications. Moreover, in the instant case, the search for the polypeptides and the methods of using the polypeptides are not coextensive. Groups III and IV encompasses molecules which are claimed in terms of 70% identical to SEQ ID NO: 1 or 3, which are not required for the searches of any of Groups XI, XII, XV and XVI. Moreover, even if the polypeptide products were known, the methods of uses the product may be novel and unobvious in view of the preamble or active steps.

Inventions V and VI and inventions VII and VIII are related as product and process of use, in part. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of

using that product (MPEP § 806.05(h)). In the instant case, the method claims recite that the detection of the polypeptides may be accomplished by the use of an antibody or a binding agent. Furthermore, the antibodies of groups V and VI can be used to modulate the activity of polypeptides to which the antibodies bind, and these methods may be in vitro methods or in vivo methods that require an in vivo administration step of the antibody.

Searching the inventions of V and VI and inventions VII and VIII together would impose serious search burden. The inventions of Groups V and VI and inventions VII and VIII have a separate status in the art as shown by their different classifications. Moreover, even if the antibody products were known, the methods of use of the products may be novel and unobvious in view of the preamble or active steps.

Inventions I and II and inventions VII and VIII, inventions XI and XII, inventions XIII and XIV and inventions XV and XVI are unrelated because the products of groups I and II are not used or otherwise involved in the processes of groups VII and VIII and groups XI and XII and groups XIII and XIV.

Inventions III and IV and inventions IX and X, inventions XI and XII, inventions XIII and XIV and inventions XV and XVI are unrelated because the products of groups III and IV are not used or otherwise involved in the processes of groups IX and X, groups XI and XII, and groups XIII and XIV.

Inventions V and VI and inventions IX and X, inventions XI and XII, inventions XIII and XIV and inventions XV and XVI are unrelated because the products of groups III and IV are not

used or otherwise involved in the processes of groups IX and X, groups XI and XII, and groups XIII and XIV.

The inventions of Groups I-XVI have a separate status in the art as shown by their different classifications. As such, it would be burdensome to search any combination of the inventions of Groups I, II, III, IV, V, VI, VII, VIII, IX, X, XI, XII, XIII, XIV, XV, XVI together.

Because these inventions are distinct for the reasons given above, have acquired a separate status in the art as shown by their different classification, and the search required for each group is not required for the other groups because each group requires a different non-patent literature search due to each group comprising different products and/or method steps, restriction for examination purposes as indicated is proper.

The examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and a product claim is subsequently found allowable, withdrawn process claims that depend from or otherwise include all the limitations of the allowable product claim will be rejoined in accordance with the provisions of MPEP § 821.04. Process claims that depend from or otherwise include all the limitations of the patentable product will be entered as a matter of right if the amendment is presented prior to final rejection or allowance, whichever is earlier. Amendments submitted after final-rejection are governed by 37 CFR 1.116; amendments submitted after allowance are governed by 37 CFR 1.312.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for

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patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103, and 112. Until an elected product claim is found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowed product claim will not be rejoined. See "Guidance on Treatment of Product and Process Claims in light of *In re Ochiai*, *In re Brouwer* and 35 U.S.C. § 103(b)," 1184 O.G. 86 (March 26, 1996). Additionally, in order to retain the right to rejoinder in accordance with the above policy, Applicant is advised that the process claims should be amended during prosecution either to maintain dependency on the product claims or to otherwise include the limitations of the product claims. Failure to do so may result in a loss of the right to rejoinder. Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

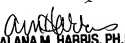
Applicant is advised that the reply to this requirement to be complete must include an election of the invention to be examined even if the requirement is traversed (37 CFR 1.143).

Any inquiry concerning this communication or earlier communications from the Office should be directed to Anne Holleran, Ph.D. whose telephone number is (571) 272-0833. Examiner Holleran can normally be reached Monday through Friday, 9:00 am to 5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew, can be reached at (571) 272-0787.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist at telephone number (703) 571-1600.

Anne L. Holleran
Patent Examiner
March 31, 2005


ALANA M. HARRIS, PH.D.
PRIMARY EXAMINER
04/04/2005